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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

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EXAMINER	

ART UNIT	PAPER NUMBER
	7

DATE MAILED: 9/17/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ Responsive to communication filed on 7/10/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire — month(s), 30 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892. ✓
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1 – 16 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☐ Claims _____ are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1–16 are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-13 and 16, drawn to a method for detecting a target cell in a cell suspension and kit.

Group II, claim 14, drawn to a method for biological analysis of cells.

Group III, claim 16, drawn to a method for inoculating an immunodeficient animal.

2. The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

The paramagnetic particles or beads coated with antibodies specific for the cells of interest used to separate the target cells from a cell suspension is not considered to be a special technical feature because, such beads and their use are well known in the art, thus the coated beads are not considered to be novel and therefore, cannot be a special technical feature of the invention.

The beads and method of using them according to claim 1 is obvious over Widder et al (EP 016,552) in view of Connelly et al (US Patent No. 5,422,277) and Forrest et al (US Patent No. 4,659,678).

Widder et al teach magnetically-responsive microspheres having Protein A associated with the surfaces and further reacted with select antibodies before the microspheres are used for cell separation (column 2, lines 48-55). Widder et al teach magnetic microspheres containing Protein A coupled with FITC-conjugated rabbit IgG by incubation at 37°C for 20 minutes and examined. The intensity and uniform distribution of fluorescence indicated that Protein A was oriented on the microspheres surface in a manner that allowed IgG molecules to interact with the Fc binding sites on the Protein A (column 6, example 1). Widder et al teach using the coated particles to separate red blood cells (RBC) from suspensions containing a mixture of different RBCs. The

RBCs are labeled with ^{51}Cr and incubated with the IgG-coated microspheres for 30 minutes at 37°C with mild agitation. Cells were separated and counted using a gamma counter (column 7, example 2).

Widder et al differ from the instant invention in failing to teach the use of enzyme labels and the avidin/biotin binding system. Widder et al also do not teach using fixatives to pretreat the sample.

Connelly et al teach various fixatives used to fix cells without destroying cellular properties. Connelly et al teach fixing cells with phosphate buffered solution followed by DMSO and DNBS, Tween™ and formaldehyde (column 9, lines 10-14). Connelly et al teach incubating the cells with the fixative for about 20 minutes to 2 hours at temperatures ranging from 0°C to about 37°C. Connelly et al teach that the fixative composition is used in the fixing of bone marrow and blood cells, and fixed cells can then be examined by any suitable technique known to the art such as through the use of a microscope, immunofluorescence or flow cytometry (column 9, lines 45-48).

Forrest et al teach a sandwich assay using solid supports such as particles or beads having labeled or unlabeled antibodies attached thereto. The label employed maybe selected from those known in the art such as fluorimetric or enzyme labeling. Forrest et al also teach using Protein A attached to the solid support and further attached to an antibody (columns 3-4). Forrest et al teach using reagents that constitute a specific binding protein such as avidin and biotin and adding the reagents in any order so as to optimize the reaction conditions (column 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to pretreat the sample of Widder et al using the fixatives taught by Connelly et al because Connelly et al teach that fixed cells are useful in monitoring blood cells for viral burden by enhancing the measurement of viral components in a sample and Widder et al teach that their method of magnetic separation is used to identify a specific cell type, bacterial or viruses, thus the fixatives of Connelly et al provide an improve method of identifying a specific component of a sample. The fixatives of Connelly et al are also useful in providing means to fix cells without destroying cellular properties thus allowing one to analyze the cells in details. It would have been

obvious to one of ordinary skill in the art at the time the invention was made to use binding system such as avidin/biotin, as taught by Forrest et al, because Forrest et al teach that avidin/biotin provides a very rapid and high affinity binding which offers the advantage that a reaction can be made very rapid and complete. The use of "double-antibody layer", i.e. Protein A-Ig, is also well known in the art and a skill artisan would have had a reasonable expectation of success in using such double layer because Widder et al teach that such microspheres are effective for antigen binding and use in magnetic sorting procedures is thereby maximized which greatly increases the efficiency with which the select antibodies may be used. It also eliminates the need for chemical coupling of the antibodies. Incubation temperature and time are easily modified by a skilled artisan to optimize reaction conditions.

3. Accordingly, the invention of Group I does not relate to the invention of Group II because they are different inventions. Group I is directed toward a method of separating a target cell from a sample, whereas Group II is directed toward different methods of biologically analyzing a sample of cells.

The invention of Group I does not relate to the invention of Group III because they are different inventions. Group I is directed toward a method of separating a target cell from a sample, whereas Group III is directed toward a method for inoculating an immunodeficient animal with cells established in vitro.

The invention of Group II does not relate to the invention of Group III because they are different inventions. Group II is a method of biologically analyzing a sample of cells, whereas as Group III is a method of inoculating an immunodeficient animal.

4. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1.

The species are as follows:

I. Normal cells expressing growth factor receptors, or Integrins, or adhesion membrane molecules or MDR proteins.

II. Normal cells expressing oncogenic products

III. Abnormal cells expressing integrins, or adhesion membrane molecules, or MDR proteins or growth factor receptors or other oncogenic products.

Applicant is required, in response to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The response must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

5. The claims are deemed to correspond to the species listed above in the following manner:

I. 2, 4, 5 and 12.

II. 3 and 12

III. 6, 10-12 and 13.

The following claim(s) are generic: 1, 7-9 and 16.

6. The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The cells of Group I do not relate to the cells of the Group II or Group III because they are different type of cells expressing different antigenic determinants.

Applicant is also reminded that with the election of the species of Group I or Group III, an election of cells expressing one of the antigens listed above must also be chosen. Further, an election of a single antigen belonging to each of the groups of adhesion molecules, or integrin or growth receptors etc., such as those listed in table 1 of the specification must also be chosen.

7. A telephone call was made to Ian McIntyre on September 3, 1996 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently

named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy Nguyen whose telephone number is (703) 308-4243. The examiner can usually be reached Monday through Friday, from 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

BTN
September 4, 1996

Christopher L. Chin

CHRISTOPHER L. CHIN
PATENT EXAMINER
GROUP 1800